Cardiovascular Health in African Americans

A Scientific Statement From the American Heart Association

Endorsed by the American College of Cardiology

BACKGROUND AND PURPOSE: Population-wide reductions in cardiovascular disease incidence and mortality have not been shared equally by African Americans. The burden of cardiovascular disease in the African American community remains high and is a primary cause of disparities in life expectancy between African Americans and whites. The objectives of the present scientific statement are to describe cardiovascular health in African Americans and to highlight unique considerations for disease prevention and management.

METHOD: The primary sources of information were identified with PubMed/Medline and online sources from the Centers for Disease Control and Prevention.

RESULTS: The higher prevalence of traditional cardiovascular risk factors (eg, hypertension, diabetes mellitus, obesity, and atherosclerotic cardiovascular risk) underlies the relatively earlier age of onset of cardiovascular diseases among African Americans. Hypertension in particular is highly prevalent among African Americans and contributes directly to the notable disparities in stroke, heart failure, and peripheral artery disease among African Americans. Despite the availability of effective pharmacotherapies and indications for some tailored pharmacotherapies for African Americans (eg, heart failure medications), disease management is less effective among African Americans, yielding higher mortality. Explanations for these persistent disparities in cardiovascular disease are multifactorial and span from the individual level to the social environment.

CONCLUSIONS: The strategies needed to promote equity in the cardiovascular health of African Americans require input from a broad set of stakeholders, including clinicians and researchers from across multiple disciplines.

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Key Words: AHA Scientific Statements ■ African Americans ■ cardiovascular diseases ■ disease management ■ prevention and control ■ risk factors

Despite advances in the identification of risk factors for cardiovascular disease (CVD) and the widespread use of evidence-based strategies to manage CVD, racial/ethnic disparities in CVD morbidity and mortality persist in the United States. Across nearly every metric, African Americans have poorer overall cardiovascular health than non-Hispanic whites, and CVD mortality is higher in African Americans than whites.[1,2] In fact, little has changed since 2005 when notable disparities in prevalence, disease management, and outcomes were reported in a special issue of *Circulation*.[3] The American Heart Association (AHA) is a leader in highlighting disparities in CVD by race and ethnicity. The present scientific statement on cardiovascular health in African Americans follows statements published on Asian Americans[4] and US Hispanic/Latinos.[5] Our intention is for the statement to be used by clinicians, public health practitioners, and policy makers to interrupt these adverse trends and to move toward cardiovascular health equity for African Americans.

SIGNIFICANCE AND RATIONALE

African Americans are the oldest nonnative racial groups in the United States, with the large initial influx coming to America involuntarily during the transatlantic slave trade. Since that time, individuals of African descent from around the world (eg, Africa, the Caribbean, Latin America) have immigrated to the United States and contribute to the diversity of language, customs, and cultures of the US African American population. In the present report, we have chosen the term African American to refer to black Americans of African descent living in the United States. However, when referencing work from studies that specifically denote the inclusion of non-Hispanic blacks, we have retained their original label. At present, African Americans make up 13.3% of the US population and are the second largest racial/ethnic minority behind Hispanic/Latinos.[6]

In 2012, the life expectancy of African Americans was 3.4 years shorter than that of whites (75.5 versus 78.9 years, respectively). The contrasts are most striking when studied by race and sex: White women have the longest life expectancy at 81.4 years, followed by black women at 78.4 years, white men at 76.7 years, and black men at 72.3 years.[7] Among the 25 leading causes of death, 6 of the 10 diseases that are substantial contributors to years of life lost are CVD risk factors (ie, hypertension, diabetes mellitus, renal disease) or CVDs (ie, ischemic heart disease, heart failure, and stroke). In the most recent report by the Centers for Disease Control and Prevention, CVDs were estimated to explain 32% of the mortality difference between African American and white men and 43% of the difference between African American and white women in 2009.[8] Together, these conditions contributed to >2.0 million years of life lost in the African American population between 1999 and 2010.

OBJECTIVES

The objectives of the current statement are to describe cardiovascular health and the burden of CVD in the population; to discuss the contribution of traditional CVD risk factors and adverse health behaviors to disparities in cardiovascular health between African Americans and whites; to describe the contribution of comorbidities that are overrepresented among African Americans to CVD; to identify and discuss genetic and biological mechanisms that might contribute to the disease pathways leading to CVD in African Americans; to highlight unique considerations (ie, differential effects of pharmacological strategies) in disease prevention and management in African Americans; and to discuss the social, cultural, and environmental factors that influence prevention and disease management in African Americans. Aside from a brief discussion about the origin of disparities in youth, the current statement focuses on health in adults. A detailed discussion of strategies to reduce disparities in CVDs between African Americans and other racial/ethnic groups is beyond the scope of the present statement. We conclude the statement by recommending a broad set of strategies for change, from additional research to workforce development.

BURDEN OF CVDs AND STROKE

The term *cardiovascular diseases* will collectively include coronary heart disease (CHD), sudden cardiac death/sudden cardiac arrest, stroke/transient ischemic attack, and peripheral arterial disease. The AHA has played a key role in summarizing trends in cardiovascular health and disease in the annual AHA statistical report.[2] Because these data are published and updated annually, we only briefly summarize the burden of these diseases in African Americans compared with non-Hispanic whites.

Coronary Heart Disease

Although the rates of CHD have declined in recent decades, those declines are smaller among African Americans than whites. In the ARIC study (Atherosclerosis Risk in Communities), the decline in CHD incidence among African American men was half (–3.2%/y) that of the decline among white men (–6.5%/y). African American women experienced a decline of –4.0%/y, whereas white women experienced a decline of –5.2%/y.[1] In 2010 (the most recent year that national prevalence rates were available), the self-reported prevalence of

Circulation. 2017;136:e393–e423. DOI: 10.1161/CIR.0000000000000534

diagnosed CHD was 6.5% in African Americans compared with 5.8% in whites, a difference that was not statistically significant. However, the modestly higher rate in African Americans is driven by the excess among African American women (5.9%) compared with white women (4.0%); among men, rates were higher among whites (7.7%) versus African Americans (7.3%).[9] Longitudinal data from the REGARDS study (Reasons for Geographic and Racial Differences in Stroke) describe no difference in incident CHD between African American and white men (hazard ratio [HR], 1.04; 95% confidence interval [CI], 0.84–1.29) and only a marginally and nonsignificantly higher incidence in African American women versus white women (HR, 1.25; 95% CI, 0.96–1.62). However, African American men and women have substantially higher rates of fatal CHD than whites (men: HR, 2.18; 95% CI, 1.24–2.56; women: HR, 1.63; 95% CI, 1.02–2.62).[10]

Heart Failure

The incidence, prevalence, and prognosis of heart failure are less favorable among African Americans and are largely attributable to the higher burden of traditional risk factors among African Americans. Disparities in the incidence of heart failure are most prominent at young ages, as reported by the CARDIA study (Coronary Artery Risk Development in Young Adults), in which 26 of the 27 incident heart failure cases that occurred in individuals <50 years of age were among black participants.[11] Although disparities in heart failure persist in middle-aged and older adults (mean age, 62 years) in MESA (Multi-Ethnic Study of Atherosclerosis; HR, 1.81; 95% CI, 1.07–3.07 in African Americans versus whites), statistical adjustment for established risk factors (ie, age, sex, diabetes mellitus, hypertension, cholesterol, smoking status, and left ventricular hypertrophy) explained all of the excess risk among African Americans versus whites (HR, 1.42; 95% CI, 0.81–2.48).[12] Findings were similar in the ARIC study, but the extended follow-up (15 versus 4 years in MESA) and large number of total events (n=1282) provided additional evidence that the disparities were present with younger age at disease onset. Among men, adjustment for established risk factors eliminated any differences in heart failure incidence between African Americans and whites (HR, 0.86; 95% CI, 0.70–1.06, African Americans versus whites). However, among women, African Americans were significantly more likely to experience events within the first 7.5 years even after statistical adjustment for risk factors (HR, 1.79; 95% CI, 1.25–2.55 versus white women). The disparity between African American and white women was attenuated only after adjustment during the second half of follow-up when women were older (HR, 0.93; 95% CI, 0.46–1.90, African American versus white). In that same study, the age-adjusted 30-day case fatality rate (per 1000 person-years) was significantly higher ($P<0.05$) in African American men (51.8; 95% CI, 44.1–59.4) and women (46.1; 95% CI, 39.8–52.5) compared with white men (41.2; 95% CI, 36.9–45.6) and white women (35.8; 95% CI, 30.6–41.4).[13]

Sudden Cardiac Arrest/ Sudden Cardiac Death

Sudden cardiac arrest, a sudden pulseless condition frequently attributable to underlying cardiac causes, has high fatality rates outside of hospital settings (ie, sudden cardiac death). Both sudden cardiac arrest and sudden cardiac death are higher in African Americans compared with whites, primarily because of a higher burden of traditional and nontraditional (eg, sickle cell trait) CVD risk factors in African Americans.[14] In the Oregon Sudden Unexpected Death Study, a community-based epidemiological study initiated in 2002 to collect information about out-of-hospital cardiac arrest, African Americans were twice as likely to experience sudden cardiac death. From 2002 to 2012, the rate of sudden cardiac arrest was 175 per 100 000 in African American men compared with 84 per 100 000 in white men. African American women experienced sudden cardiac death at a rate of 90 per 100 000, whereas white women experienced sudden cardiac arrest at a rate of 40 per 100 000. African American men and women who experienced sudden cardiac arrest were on average >6 years younger than their white counterparts. According to the National Registry on Cardiopulmonary Resuscitation, when patients are hospitalized for sudden cardiac arrest, African Americans are less likely to survive to discharge (25.2%) than whites (37.4%).[15]

Cerebrovascular Disease/Stroke

Cerebrovascular disease incidence and mortality, inclusive of transient ischemic attacks, ischemic stroke, and intracerebral hemorrhage, are notably higher in African Americans compared with whites in the United States. Notably, although stroke mortality has fallen by 80% across all ages over the past 60 years, there has been no meaningful decrease in the magnitude of the African American to white racial disparity in stroke mortality.[16] Since the earliest studies in the 1950s, stroke mortality rates in nonwhites (predominately African Americans) remain 4.5-fold higher than among whites. Whether the higher stroke mortality in African Americans is attributable to a higher incidence of stroke, higher case fatality after stroke events, or a combination is not entirely known. In the ARIC study, the incidence rate ratio for stroke comparing African Americans to whites <55 years of age was modestly larger (relative risk [RR], 2.77; 95% CI, 1.37–5.62) than the same comparison in those >55 years of age (RR, 2.23; 95% CI, 1.66–3.00).[17]

However, most African Americans in ARIC were recruited from a single clinical site in the southern Stroke Belt region (Jackson, MS), confounding the racial and geographic disparities in stroke risk and complicating the interpretation of these results. The implication of the regional differences in the racial disparity in magnitude is that the Stroke Belt is more "potent" for African Americans than whites, and as a corollary, it is possible that between 2% and 13% of the black-white difference in stroke risk (and likely coronary risk) is a result of confounding with geographic differences in risk.[18]

Data from both REGARDS and GCNKSS (Greater Cincinnati/Northern Kentucky Stroke Study) have shown that age-related differences in the magnitude of racial disparity in stroke mortality are mirrored by age-related changes in the magnitude of the racial disparity in stroke incidence. GCNKSS reported patterns of stroke incidence in 1999 in the Cincinnati region that were similar to the national pattern for stroke mortality, with stroke mortality 2.6 times greater in African Americans than whites at 45 to 54 years of age but decreasing to 1.8 times for 55 to 64 years of age, 1.2 times for 65 to 74 years of age, 0.9 times for 75 to 84 years of age, and 0.8 times for ≥85 years of age.[19] In the same report, stroke case fatality was 24% lower in African Americans than whites, an observation that was relatively consistent across stroke subtypes of infarction and hemorrhage.[19]

There is a strong age-related difference in the risk of intracerebral hemorrhage in African Americans compared with whites. At 55 to 74 years of age, African Americans were 1.8 times more likely to experience intracerebral hemorrhage, but that difference was only modestly greater (RR, 1.23 times) for ages ≥75 years.[20] A pooled analysis of ARIC and the CHS (Cardiovascular Health Study) showed a similar pattern whereby the RR of intracerebral hemorrhage for African Americans versus whites was 5.8 at 45 years, 1.7 at 65 years, and 0.94 at 75 years of age.[21] Among 45- to 64-year-olds in REGARDS, the incidence rate of intracerebral hemorrhage (per 100 000) was doubled for African Americans (46.0; 95% CI, 26.5–79.7) compared with whites (21.5; 95% CI, 11.2–41.2). However, these associations were reversed in older adults. The risk of incident intracerebral hemorrhage was 40.1 (95% CI, 17.8–90.4) in African Americans and 65.1 (95% CI, 39.1–108.4) in whites 65 to 74 years old. At ages ≥75 years, the incidence rates were 65.8 (95% CI, 24.4–177.8) in African Americans and 105.0 (95% CI, 64.3–171.3) in whites.[22]

Peripheral Arterial Disease

Atherosclerotic disease affecting the arteries and vessels outside of the heart, peripheral arterial disease/peripheral vascular disease, is a common geriatric disease with a prevalence of 12% to 20% among adults >80 years of age.[23] Across the age range, the rate of peripheral arterial disease is twice as high in African Americans compared with whites.[24] Traditional risk factors, namely cigarette smoking, diabetes mellitus, and hypertension, are the strongest risk factors for peripheral arterial disease, but statistical adjustment for these and other traditional risk factors does not completely eliminate the excess prevalence in African Americans compared with whites.[25,26] In the MESA study, the adjusted odds for incident peripheral arterial disease were 1.67 times higher in African Americans compared with whites.[27] The San Diego Population Study included markers of inflammation in multivariable models to test whether they explained the residual excess risk in African Americans compared with whites but found that, although the RRs for peripheral artery disease between African Americans and whites were further attenuated, they remained statistically significantly higher, ranging from 1.5 to 2.0.[28]

Although peripheral arterial disease is not considered a direct cause of mortality but rather a reflection of the overall burden of CVD, peripheral arterial disease was listed as the underlying cause of death for 59 681 deaths in 2014. The any-mention age-adjusted death rate resulting from peripheral arterial disease was higher among African American men (24.8 per 100 000) than white (19.9), American Indian or Alaska Native (20.8), Hispanic (15.4), or Asian Pacific Islander (8.5) men. Similar patterns of peripheral arterial disease mortality were observed for African American women (16.5) compared with white (13.8), American Indian or Alaska Native (16.1), Hispanic (10.7), and Asian or Pacific Islander (6.8) women.[2]

Summary

There are marked disparities in the onset of heart failure, stroke, and peripheral vascular disease between African Americans and whites, whereas rates of CHD are not significantly different, particularly among men. However, mortality from all CVDs is significantly higher in African Americans compared with whites, which suggests a role for health care to mitigate disparities with comprehensive screening, an enhanced specificity of diagnoses, and tailored disease management. The prominence of disparities in the onset of CVD at younger ages highlights the contribution of cardiovascular risk factors and adverse health behaviors among African Americans.

TRADITIONAL CVD RISK FACTORS

The AHA 2020 Strategic Impact Goals for Cardiovascular Health Promotion and Disease Reduction provided metrics to determine adherence to current recommendations for CVD prevention. Subsequent reports

Circulation. 2017;136:e393–e423. DOI: 10.1161/CIR.0000000000000534

identified African American children, adolescents, and adults[30,31] as less likely than other racial/ethnic groups to achieve ideal cardiovascular health. The following sections describe the burden of cardiovascular risk factors, proposed risk factor management, and adverse health behaviors.

Cardiovascular Risk Factors

Hypertension

Hypertension is arguably the most potent risk to the cardiovascular health of African Americans, as well as the greatest area of opportunity for the prevention of disease if effectively managed and prevented. The prevalence of diagnosed and undiagnosed hypertension among African American men (42.4%) and women (44%) ≥20 years of age in the United States[32] is among the highest in the world where the population prevalence of hypertension is the highest in low- to middle-income countries (29%–31%).[33] An analysis of trends indicates that rates of hypertension among African Americans remained ≈10% to 12% higher than rates among non-Hispanic whites and Mexican Americans since 1999 to 2000 (the year that the National Health and Nutrition Examination Survey [NHANES] became semiannual).[32] Percent of African admixture in African Americans and other racial/ethnic groups is positively associated with blood pressure (BP) levels and the prevalence of hypertension.[34,35]

The origins of adult differences in hypertension begin in youth. African American boys and girls have higher BP levels and a higher prevalence of hypertension (13.8% in African Americans versus 8.4% in whites and 10.4% in Hispanics).[36] Findings from the Bogalusa Heart Study indicate that higher BP levels during childhood track into elevated BP in adults.[37] These differences persist into older ages, as evidenced by the MESA study, in which the odds of hypertension were 1.5 times higher in African Americans than in whites through age 75 years.[38] In REGARDS, the RR of incident hypertension was 1.24 (95% CI, 1.12–1.37) times higher in African American men compared with white men across the life span. In contrast, an interaction with age was observed for women (P=0.08). The RR for incident hypertension was significantly higher for African American women 65 to 74 years of age (RR, 1.44; 95% CI, 1.24–1.66) but was not significant for age >75 years (RR, 1.18; 95% CI, 0.84–1.65, African American versus white women).[39]

On a positive note, African Americans were more likely than whites or Hispanics to be aware of their hypertension and to have it treated.[40,41] In NHANES, 87% of African Americans, 81% of whites, and 77% of Hispanics were aware of their hypertension, and 80% of African Americans were treated with medications compared with 77% of whites and 70% of Hispanics.[40] African Americans in REGARDS were also more likely to be aware of their hypertension (odds ratio [OR], 1.45; 95% CI, 1.24–1.71 versus whites) and treated (OR, 1.56; 95% CI, 1.34–1.83, African Americans versus whites).[42] Despite these favorable trends in awareness and treatment as noted in NHANES, fewer African Americans achieve BP control (47.9%) than non-Hispanic whites (56%).[40] Similarly, the adjusted odds of hypertension control in REGARDS are lower in African Americans compared with whites (OR, 0.67; 95% CI, 0.60–0.74).[42]

The prevalence of hypertension in African Americans has significant implications for mortality. The magnitude of the association between systolic BP (SBP) levels and stroke risk is 3 times greater in African Americans than in whites; a 10–mm Hg difference in SBP is associated with an 8% (95% CI, 0–16) increase in the stroke risk in whites but a 24% (95% CI, 14–35) increase in African Americans. Within strata of SBP, stroke risk goes up with an increasing number of classes of antihypertensive medications used to treat high BP (RR, 1.42 for 1 class up to 2.48 for ≥3 classes).[43] Even when treatment recommendations are followed for African Americans, stroke risks remain elevated, suggesting primordial prevention as the best strategy to eliminate the risks of hypertension-related vascular outcomes.

The National Heart, Lung, and Blood Institute (NHLBI) Working Group on Research Needs to Improve Hypertension Treatment and Control in Africans produced a brief report summarizing some of the above findings and, above all, advocating for additional research into the sources of disparities in hypertension control in African Americans, given its contribution to significant disparities in CVDs.[44] Consequently, addressing disparities in hypertension incidence and management is a high priority.

Diabetes Mellitus

More than 95% of the cases of diabetes mellitus are classified as type 2,[45] and the combined prevalence of diagnosed and undiagnosed type 2 diabetes mellitus is 14.3% overall but 21.8% in African Americans and 11.3% in non-Hispanic whites according to NHANES 2011 to 2012.[46] More than 1 in 3 (37%) African Americans with diabetes mellitus were not diagnosed.[46] The prevalence of diabetes mellitus among African Americans has increased dramatically in the past decades, from 8% in 1988 to 1994 to the current rates.[46] Similarly, prediabetes increased among African Americans from 14% in 1988 to 1994 to 20% in 2005 to 2010.[47] The elevated incidence of diabetes mellitus among African Americans extends over the life course, with no age-related decline in the disparity. Over a lifetime, African American men develop diabetes mellitus 1.52 times (95% CI, 1.31–1.78) more often than white men, and African American women are 2.14 (95% CI, 1.86–2.46)

times more likely to develop diabetes mellitus than white women.[39]

Although type 1 diabetes mellitus remains the most common type of diabetes mellitus among children and adolescents (age <21 years), rates of type 2 diabetes mellitus among youth have increased secondary to the obesity epidemic. African American adolescents (age, 12–19 years) are significantly more likely to develop diabetes mellitus than whites, and their rate falls short of only the rate among American Indian adolescents.[48] These patterns are particularly troublesome given the long lifetime of exposure to higher glucose levels among African Americans that contribute to mortality and vascular complications of diabetes mellitus.

The diagnosis of diabetes mellitus is made by a combination of fasting glucose, postchallenge glucose, and hemoglobin A_{1c}.[45] However, relying solely on hemoglobin A_{1c} could underestimate the prevalence of diabetes mellitus in African Americans because of disorders such as sickle cell trait that occur among individuals of African ancestry. Recent research indicates that at a given level of fasting glucose, hemoglobin A_{1c} is statistically significantly lower (5.72%) among those with sickle cell trait versus those without (6.01%).[49] Delays in diagnosing diabetes mellitus have adverse implications for the development of vascular complications.

African Americans are less likely to be aware of their diabetes mellitus and, when treated, are less likely to achieve adequate control according to common quality metrics defined by the Accountable Care Organization (hemoglobin A_{1c} <9%).[50] Only 54% of African Americans achieved targets compared with 61% of whites,[47] which may contribute directly to the elevated excess in microvascular complications of diabetes mellitus in African Americans compared with whites.[51] The age-adjusted death rate among people with diabetes mellitus in 2011 was 40 per 100 000 in African Americans compared with 19 per 100 000 in whites and 26 per 100 000 in Hispanics.[52] Compared with their white peers, African Americans with diabetes mellitus are 4 times more likely to have visual impairment (caused by diabetic retinopathy)[53] and 3.8 times more likely to have end-stage renal disease (resulting from diabetic nephropathy)[54,55] but possibly less likely to experience lower extremity amputation.[56]

Lipid Disorders

Despite higher atherosclerotic CVD (ASCVD) rates and higher mortality from CHD among African Americans, lipid profiles among African Americans according to national prevalence estimates are comparable to or lower than those of non-Hispanic whites. For example, the prevalence of elevated total cholesterol (≥200 mg/dL) was 37.0% in non-Hispanic white males versus 32.6% in non-Hispanic blacks in NHANES 2011 to 2014. Comparable percentages of elevated total cholesterol among women were 43.4% among non-Hispanic whites and 36.1% in non-Hispanic blacks.[2] High-density lipoprotein (HDL) cholesterol is known to be higher in African Americans, and in recent estimates from NHANES, those patterns hold, with the prevalence of low HDL (<40 mg/dL) at 28.4% in non-Hispanic white men compared with only 20.7% in non-Hispanic black men. There were small differences in the prevalence among women (10.3% in non-Hispanic white women and 8% in non-Hispanic black women).[2] The prevalence of dyslipidemia was higher among African Americans in the JHS (Jackson Heart Study), a cohort in Jackson, MS, compared with national estimates. One third of participants 35 to 84 years of age had hypercholesterolemia, defined as total cholesterol ≥240 mg/dL, low-density lipoprotein (LDL) cholesterol (LDL-C) ≥160 mg/dL, or triglycerides ≥200 mg/dL.[57] In this population, the most common dysfunction was in elevated LDL-C (18.3%), followed by total cholesterol (15.2%) and then triglycerides (5.4%).[57] Relying on the lipid panel and a focus on dyslipidemia may underestimate CVD risk in African Americans given the relatively lower likelihood of high LDL-C and triglycerides in African Americans. However, incidence data on dyslipidemia present a different picture.

Over the age of 45, there is a higher incidence of dyslipidemia (total cholesterol ≥240 mg/dL, LDL ≥160 mg/dL, HDL ≤40 mg/dL, or use of lipid-lowering medications) in African American men (RR, 1.15; 95% CI, 1.04–1.28) and women (RR, 1.17; 95% CI, 1.08–1.28) than in their white counterparts. However, among both men (P=0.10) and women (P=0.02), the disparities become even more pronounced in older ages, with the RR of dyslipidemia in African American men compared with white men increasing from 1.15 (95% CI, 0.82–1.61) at 45 to 54 years of age to 1.26 (95% CI, 1.06–1.51) at 65 to 74 years of age. The RR of dyslipidemia for African American women versus white women is 0.97 (95% CI, 0.77–1.22) at 45 to 54 years of age but 1.39 (95% CI, 1.00–1.95) among women ≥75 years of age.[39] The apparent contradiction in findings between prevalence and incidence may be explained by the higher rates of CVD mortality among African Americans compared with whites. Disease prevalence is determined on the basis of a combination of disease incidence and the average duration of disease. If African Americans are more likely to die of CVD that could be attributed to dyslipidemia, then the burden of dyslipidemia would not be captured in prevalence estimates because they are exiting the denominator before their disease is captured. Consequently, dyslipidemia management is critically important.

Although the introduction of statin therapy has revolutionized the treatment of lipid disorders, the introduction of therapy requires CVD risk assessment. At the baseline examination of the JHS in 2000 to 2003,

Circulation. 2017;136:e393–e423. DOI: 10.1161/CIR.0000000000000534

69.7% of participants were aware that they had hypercholesterolemia, 43% of those were being treated, and among those, 88% were controlled.[57] In the REGARDS study, African Americans were less likely to be aware of their dyslipidemia (OR, 0.69; 95% CI, 0.61–0.78), less likely to have their dyslipidemia treated (OR, 0.77; 95% CI, 0.67–0.89), and if treated, less likely to have their lipids under control (OR, 0.67; 95% CI, 0.58–0.77).[58]

Findings from MESA suggested that guideline-recommended treatment was underused in all ethnic groups examined.[59] The lowest control rates of dyslipidemia among those on lipid-lowering therapy were seen among African American women (65.7% controlled versus 86.2% for non-Hispanic white women), followed by African American and Hispanic men (both 68.5% versus 76.4% in non-Hispanic white men).[59] Although the guidelines have been updated to eliminate numerical targets as therapeutic goals,[60] the historical pattern of undertreatment among African Americans[57,59] raises the concern that without specific attention by providers and adherence by patients, CVD risk tied to dyslipidemia will remain higher among African Americans than other Americans.

Obesity

Across the age spectrum, obesity rates are higher among African Americans than whites. One in 5 (20%) African American children 2 to 19 years old were obese (defined by a body mass index [BMI] for age value ≥95th percentile of the 2000 Centers for Disease Control and Prevention growth charts) compared with 15% of whites. The rates of extreme obesity (BMI for age value ≥120th percentile of the 2000 Centers for Disease Control and Prevention growth charts) in children were more than double in African American children (9%) compared with whites (4%).[61,62] Among adults ≥20 years of age, African American women had the highest rates of obesity (BMI >30 kg/m^2) at 58%, followed by African American men (38%), white men (34%), and white women (33%).[2] The prevalence of severe obesity (BMI ≥40 kg/m^2) among African Americans (12.1%) was double that of the next highest groups (Hispanics, 5.8%, and whites, 5.6%).[62]

The obesity paradox, the observation of a higher risk of mortality in leaner and normal-weight individuals than among adults who are overweight or have class I obesity,[61] may warrant investigation among African Americans. Previous findings from a large cohort study, the Cancer Prevention Study II, showed only a moderately elevated risk of all-cause mortality with increased weight among African Americans but a much stronger finding among whites.[63] There are several potential explanations for the observation of an obesity paradox that fall outside of the scope of the present review (eg, selection bias, reverse causation, residual confounding, and measurement error[64]). One that is potentially most relevant to African Americans is error arising from the use of BMI to represent adiposity.

Although the most common metric to define obesity clinically and at the population level is BMI, body composition and body fat distribution are more precise indicators of metabolic and cardiovascular risk. NHANES captured waist circumference and found that African American women have a larger waist circumference compared with white women but that there were no differences between African American and white men.[65] Smaller studies that have direct measures of adiposity via imaging (ie, dual x-ray absorptiometry or computed tomography) describe contradictory findings for body composition and adiposity distribution. In studies that have images of adiposity distribution within regions of the body, African American men and women have less metabolically active abdominal visceral adipose tissue compared with whites after adjustment for total body fat.[66–68] Recent findings from the Pennington Center Longitudinal Study confirm prior observations and report that African American women and men had significantly higher subcutaneous adipose tissue, which is considered protective, compared with white women and men.[69,70] However, another study found that these racial differences were reversed after adjustment for total body fat, indicating that African American men had more subcutaneous adipose tissue at a given level of total body fat.[70]

Qualitative and quantitative research on the ideal body size and shape in African Americans describes cultural attitudes that favor a larger body size, particularly for women.[71] These attitudes among African Americans complicate the acknowledgement of awareness about obesity and willingness to engage in weight management programs.[72,73] In the CARDIA study, obese women who perceived themselves as obese lost 0.09 BMI units annually over 13 years compared with obese women who perceived themselves as normal weight, who gained 0.31 BMI units annually (P<0.001).[74] In a weight-loss study, African American women made a similar number of attempts to lose weight but set a weight-loss goal that was 10 lb higher than the goal set by equally obese white women.[75]

Atrial Fibrillation

Although atrial fibrillation has long been recognized as a potent risk factor for stroke,[76,77] data from REGARDS recently documented that atrial fibrillation is also a potent risk factor for myocardial events,[78] a finding confirmed in ARIC[79] and in a meta-analysis of observational studies and clinical trials.[80] Despite African Americans having more risk factors for the development of atrial fibrillation, studies have consistently documented a lower prevalence of either self-reported or electrocardiographically defined atrial fibrillation, the so-called atrial fibrillation paradox.[81] The incidence of

atrial fibrillation increases dramatically with age, but the risk of incident atrial fibrillation is ≈0.20 to 0.50 times lower in African Americans than in their white counterparts across the adult age spectrum.[39,82,83] Data from REGARDS suggest that these benefits of a lower prevalence (and incidence) of atrial fibrillation among African Americans are offset by a much lower odds of awareness of atrial fibrillation (OR, 0.32; 95% CI, 0.20–0.52) and the fact that, if aware, African Americans are much less likely to be on treatment with warfarin (OR, 0.28; 95% CI, 0.13–0.60).[84]

Adverse Health Behaviors

Poor Diet Quality

The current guidelines for lifestyle management from the AHA and American College of Cardiology to reduce cardiovascular risk include consuming a dietary pattern that emphasizes fruits, vegetables, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils, and nuts; and limits intake of sweets, sugar-sweetened beverages, and red meats.[60] It is difficult for all Americans to meet these dietary recommendations, and adherence has been documented as low.[85] African Americans face unique challenges to adherence to recommendations. One such challenge is food intake preferences that align with a cultural tradition of "soul food." The traditional soul food diet has components that are healthful and many components that are suboptimal.[86] An example of a healthful component is the inclusion of many fruits and vegetables such as collard greens, sweet potatoes, tomatoes, dried beans and peas, watermelon, blackberries, corn, and okra. Conversely, the diet can also be described as being high in added fats, sugars, and sodium, with prominent use of high-fat meats for main dishes and the use of deep frying and other cooking techniques that add excess calories and sodium.

Regardless of their geographic residence in the United States, REGARDS has shown that African Americans are much more likely to consume a "southern diet."[87] When adherence to a southern diet was categorized into quartiles, only 9% of African Americans fell within the lowest quartile of adherence, and 60% fell within the uppermost quartile. The HR for incident CHD and stroke was elevated in the highest versus the lowest quartile of adherence (CHD: HR, 2.00; 95% CI, 1.53–2.61[88]; stroke risk: HR, 1.39; 95% CI, 1.05–1.84).[87] Adjustment for this diet score was associated with a 63% mediation of the magnitude of estimated increased risk of stroke in African Americans <65 years of age.[87,88]

Physical Inactivity

Current physical activity recommendations state that adults should engage in 150 min/wk of moderate-intensity aerobic physical activity or 75 minutes of vigorous-intensity aerobic physical activity and ≥2 d/wk of muscle-strengthening activities.[89] Data suggest that adherence to the recommended activity levels is particularly low among African Americans.[90] Fewer than 5% of all adults engaged in 30 minutes of moderate-intensity physical activity on most days of the week. Data from the CARDIA cohort show that more than one third of African American men and women report watching ≥4 hours of television per week, and this behavior is inversely associated with physical activity.[91]

When accelerometry is used to assess physical activity levels and sedentary behavior, patterns by race/ethnicity are less clear. In the NHANES study, there were no differences in minutes per day of moderate to vigorous activity between African Americans and whites.[90] Similarly, there was no difference in objectively determined sedentary behavior between African American and white men and women.[92] In the REGARDS study, only 20% of African American men and 12% of women achieved >150 min/wk of accelerometer-determined moderate to vigorous physical activity per week compared with 30% and 20% of their white counterparts ($P<0.05$).[93] African Americans also spent statistically significantly more time engaged in sedentary behaviors as assessed by accelerometry in REGARDS (735±3 minutes for African American men versus 719±2 minutes for white men; 741±2 minutes for African American women versus 730±2 minutes for white women).[93]

Cultural norms that influence behaviors, beliefs, and attitudes about physical activity are notable barriers to the adherence to physical activity recommendations. Some of these barriers include the perception that physical activity is "work" and not desired given the manual nature of daily jobs,[94] the lack of consistency between certain types of physical activity and African American self-identity (eg, double-dutch jump rope versus skiing),[95] and a low desirability for certain activities (eg, water sports) because of the physical nature,[96] the level of exertion or preparation required,[97,98] and concerns about hairstyles, particularly among women.[99] Income is another proposed barrier to meeting physical activity guidelines,[100] but the role of income varies by geography in that it is a greater concern among rural adults[100] and less so among urban African Americans.[101] Interpersonal barriers (eg, childcare, other family care), concerns about neighborhood safety, lack of access to facilities, and weather are also notable.[99] A significant limitation of the research on barriers to activity is that the vast majority has been conducted in African American women, and it is not known whether the same concerns are a priority among African American men.

Cigarette Smoking

Cigarette smoking is a strong and consistent risk factor for all CVDs, with little evidence of a differential magnitude of effect in African Americans and whites.[102] Since

the height of smoking behavior during the 1960s, rates have declined across all racial/ethnic groups to current levels of 25.4% in African Americans and 25.8% in whites.[103] However, there are important age-related differences in the prevalence of cigarette smoking by race. Although cigarette smoking is markedly higher in white than African American adolescents (18.6% versus 8.2%, respectively),[104] these differences shrink considerably among adults >25 years of age.

Two primary areas of smoking-related disparities are exposure to environmental tobacco smoke (ie, secondhand smoke) and lower quit rates among African Americans. Environmental tobacco smoke is an established cardiovascular risk factor.[105] African American members of a health practice plan reported more environmental tobacco smoke exposure than whites,[106] and African American respondents to the NHIS (National Health Interview Survey)[107] and NHANES III[108] reported more environmental tobacco exposure. One hypothesis for the lower quit rates among African Americans than whites is that they are more likely to use menthol smoking products, which enhance the addictive potential of nicotine.[109] Tobacco companies target the marketing of mentholated products to African Americans (and youth),[110] and among those smokers switching from mentholated to nonmentholated products, African Americans are more likely to revert back to the use of mentholated products.[111] Data from the Tobacco Use Supplement to the Current Population Survey report greater use of mentholated products among African American smokers (71%; 95% CI, 70.4–73.2) than white (21.0%; 95% CI, 20.5–21.4) or Hispanic (28.1%; 95% CI, 26.6–29.7) smokers. Smokers of mentholated products (of all races/ethnicities) were less likely to have quit.[112]

Clinical Sleep Disorders, Insufficient Sleep, and Poor-Quality Sleep

The relevance of sleep quality and duration on cardiovascular health was summarized in a 2016 AHA scientific statement.[113] A growing body of research describes racial/ethnic disparities in sleep-disordered breathing, sleep duration, and sleep quality. Sleep has been hypothesized as a contributing factor to disparities in CVDs.[114] African Americans are more likely to have obstructive sleep apnea (secondary to obesity),[115] and untreated sleep apnea is associated with higher rates of cardiovascular mortality from CHD or stroke directly (eg, oxygen deprivation, sympathetic overreactivity, or inflammation[116]) or through the onset of other CVD risk factors such as hypertension or diabetes mellitus.[117]

Sleep duration is associated with cardiovascular risk factors and all-cause mortality; both short and long sleepers experience higher rates of events than those who sleep on average for 7 to 9 hours per night.[118,119] African American respondents to the NHIS were 41% more likely to self-report being short sleepers and 62% more likely to report being long sleepers than white participants.[120] African American participants reported longer sleep latency (time to fall asleep) and other adverse sleep symptoms than white and Hispanic participants.[121] In the Chicago Area Sleep Study, a population-based epidemiological study of adults who underwent objective assessment of sleep via wrist actigraphy, the average sleep duration among African Americans was statistically significantly shorter per night (by ≈48 minutes) than among whites.[122] A later report in the same cohort estimated that 11% of the disparity in hypertension prevalence between African Americans and whites was attributable to poor sleep quality (as determined by the percent of time during the sleep interval spent sleeping).[123]

Multiple factors have been studied in relation to both short and long sleep duration in the all–African American JHS. Lower levels of education are associated with a greater likelihood of long sleep duration (OR, 2.19; 95% CI, 1.42–3.38). Similar findings were reported for the association of income with long sleep duration. Notably, individuals living in neighborhoods where they reported more neighborhood violence had shorter sleep duration (–9.82 minutes; 95% CI, –16.98 to –2.66) and poorer sleep quality.[124] In a later report, African American participants who reported higher levels of long-term stress were more likely to have short sleep duration (OR, 2.87; 95% CI, 2.02–4.08 versus the lower 3 quartiles of stress).[125]

Less is known about racial differences in the impact of sleep duration and cardiovascular risk. Although long sleep duration appears to be a consistent risk factor for stroke, early indications suggest that among diabetic adults, short sleep duration (≤6 hours) is associated with increased stroke risk in whites (OR, 1.38; 95% CI, 1.06–1.80) but not in African Americans (OR, 0.86; 95% CI, 0.58–1.26).[126] Additional research is needed to test the association of objectively determined sleep duration with incident CHD risk in African Americans compared with whites.

Summary

There are significant disparities in the age of onset and prevalence of established CVD risk factors in African Americans. An earlier age of onset of obesity, hypertension, and diabetes mellitus is likely to contribute to the higher prevalence of these conditions and of CVD morbidity and mortality and to the lower life expectancy for African Americans versus whites. Adverse health behaviors in the African American population identified in the literature may explain in part the higher burden of CVD risk factors. Effective implementation of evidence-based guidelines could improve cardiovascular health and lower vascular risk in African Ameri-

cans. Ingrained cultural preferences and attitudes, as well as the social and physical context surrounding African Americans, influence the maintenance of behavior changes. Furthermore, experience shows that interventions targeting individuals are modestly successful during the period of intervention, but changes are not sustained beyond the intervention period. Consequently, population-wide strategies to influence health behavior change, as described in the AHA Community Guide for Prevention,[127] may have greater potential to reach both African American women and men and to shift the health behaviors and consequent cardiovascular risk of the entire population.

COMORBIDITIES

Certain health conditions that predispose to CVDs are more common among African Americans than whites. Below, we highlight chronic kidney disease, sickle cell disease/sickle cell trait, and HIV, given their relatively higher prevalence among African Americans.

Renal Disease (Chronic Kidney Disease and End-Stage Renal Disease)

The prevalence of chronic kidney disease, determined as estimated glomerular filtration rate <60 mL·min^{-1}·1.73 m^{-2} or albuminuria,[128] has increased in the United States according to NHANES data.[129,130] African Americans have an excess burden of chronic kidney disease, resulting in part from the high prevalence of hypertension and diabetes mellitus,[131,132] but that may also be the result of the percent of African admixture and other genetic factors.[131,133,134] One such factor that has a higher prevalence in African Americans is sickle cell trait (discussed below), which has been associated with a higher rate of albuminuria and chronic kidney disease. Sickle cell trait carrier status was associated with 1.79 times higher (95% CI, 1.45–2.20) likelihood of developing chronic kidney disease over follow-up.[135]

In a pooled analysis of the ARIC and CHS studies, the risk factor–adjusted HR for all-cause mortality in African Americans with versus without chronic kidney disease was 1.76 (95% CI, 1.35–2.31), whereas the HR for the same comparison among whites was significantly smaller (HR, 1.13; 95% CI, 1.02–1.26).[136] In the REGARDS study, African Americans with mild chronic kidney disease (10 ≤albumin/creatinine ratio <30) versus no chronic kidney disease (albumin/creatinine ratio <10) were more likely to experience CHD mortality (HR, 1.84; 95% CI, 1.34–2.53) than whites (HR, 1.23; 95% CI, 0.96–1.59). The disparities grew with severity of chronic kidney disease, and among participants with severe chronic kidney disease (albumin/creatinine ratio ≥300), the HRs were 3.21 (95% CI, 2.02–5.09) in African Americans and 1.49 (95% CI, 0.80–2.76) in whites.[137] There was also evidence of effect modification in the relationship of albumin/creatinine ratio with stroke risk by race in REGARDS. The albumin/creatinine ratio was not associated with stroke risk among whites (P>0.05), but among African Americans, the HR for a stroke event was 1.41 (95% CI, 1.01–1.96) for those with mild chronic kidney disease, 2.10 (95% CI, 1.48–2.99) for those with moderate chronic kidney disease, and 2.70 (95% CI, 1.58–4.61) for those with severe chronic kidney disease.[138]

There are a number of paradoxical associations related to chronic kidney disease and end-stage renal disease among African Americans. The likelihood of progressing from chronic kidney disease to end-stage renal disease is greater in African Americans than whites.[139] Almost one third (32%) of the patients with end-stage renal disease are African American.[140] However, once on dialysis, survival is better among African Americans compared with whites. In 2008, the mortality rate for patients on dialysis was 16% in African Americans compared with 24% in whites.[140] Better survival on dialysis stands in contrast to the shorter life span for predialysis African Americans.[141] A recent study also explored inflammation as a possible explanation for this observed paradox and found that this racial difference in end-stage renal disease survival did not exist at low levels of inflammation but is present at higher levels of inflammation as reflected by the upper tertile of C-reactive protein (CRP; >9.6 mg/L).[142]

Sickle Cell Disease and Sickle Cell Trait

Sickle cell disease is a recessively inherited genetic condition caused by a glutamic acid to valine mutation in position 6 of the β-globin chain resulting in hemoglobin S formation. Subsequent sickling of red blood cells results from hemoglobin S–induced β-chain polymerization of hemoglobin tetramers.[143] Approximately 100 000 Americans have sickle cell disease, accounting for 1 in every 365 black births. However, 8% to 12% of African Americans carry a single mutation and have sickle cell trait. Although pulmonary complications and associated acute chest syndromes are the primary cardiopulmonary manifestations of sickle cell disease, there are vascular, thrombotic, metabolic, and myocardial complications of sickle cell disease and sickle cell trait.[144]

Sudden death among patients with sickle cell disease is relatively high, with an incidence as high as 41% in some studies.[145] Patients with sickle cell disease have a variety of electrocardiographic abnormalities associated with malignant electric problems, including prolonged QTc, which may predispose to arrhythmias.[146] However, published reports of continuous electrocardiographic recordings in patients with sickle cell disease remain rare, and as a result, the effect of cardiac rhythm on

mortality in these patients is unknown. Emerging research also suggests that adults with sickle cell disease may have an imbalance of autonomic function, with a relative excess of sympathetic tone that might affect the initiation and progression of vaso-occlusive crisis, reflected by a propensity for arrhythmias, impaired cardiac perfusion, and an adverse hemodynamic profile.[147]

Less is known about the cardiovascular risks for African Americans with sickle cell trait. There were no differences in the onset of CVD risk factors in a comparison of African American participants with and without sickle cell trait in the CARDIA study.[148] However, sickle cell trait was associated with an increased incidence of ischemic stroke in the ARIC study (HR, 1.4; 95% CI, 1.0–2.0).[149] In addition, emerging data suggest that African American athletes with sickle cell trait are at high risk for sudden death.[150] In a meta-analysis of the REGARDS, ARIC, MESA, JHS, and WHI (Women's Health Initiative) studies, sickle cell trait status was not significantly associated with incident myocardial infarction (HR, 1.10; 95% CI, 0.73–1.64) but was associated with CHD (HR, 1.42; 95% CI, 1.02–1.98) in a comparison of those with and without sickle cell trait.[151] Further research on mechanisms and pathways is needed to explain the discrepancy between the 2 related outcomes.

HIV/AIDS

One of the emerging triumphs of 20th century medicine is the transformation of HIV/AIDS infection from a fatal condition to a chronic illness largely attributable to the introduction of highly active antiretroviral therapy. As a result, an increasing number of individuals with HIV infection are living longer and developing various cardiovascular conditions attributable to medications and the underlying inflammatory pathophysiology of HIV. A 2008 scientific statement[152] presented evidence for the association of HIV with CVDs. Unfortunately, African Americans remain disproportionately affected by HIV infection, accounting for ≈40% of the 1.2 million individuals living with HIV in the United States, and have the highest prevalence compared with other racial/ethnic groups.[153]

A few studies include enough African American and white patients with HIV to evaluate the possibility of a differential effect of HIV on cardiovascular outcomes. In a systemic review of African Americans with HIV/AIDS in the United States, 2 of 5 studies indicated that African Americans with HIV were at increased CVD risk.[154] One of the few large assessments of CVD in African Americans with HIV is derived from a retrospective analysis of US National Hospital Discharge Surveys (1996–2008) showing that of 1.5 million discharges, the likelihood of hospitalization for CVD conditions was almost 50% higher (OR, 1.45; 95% CI, 1.39–1.51) in African Americans than in whites.[155] However, an unexpected observation that warrants further investigation is that, when the subclinical coronary artery disease burden was compared between African American men with and without HIV in MACS (Multicenter AIDS Cohort Study), HIV positivity was associated with lower volume of total plaque.[156]

Pharmacotherapy to manage HIV may increase the risks of CVDs. Although race-specific data were not presented, HIV-positive adults tend to have more dyslipidemia, characterized as high triglycerides and low HDL cholesterol (HDL-C) levels, likely as a result of decreased cholesterol ester transfer protein activity[157] compared with HIV-negative individuals. In the PURE study (Prospective Urban and Rural Epidemiology), patients with CD4 counts ≤200 cells/mm^3 who were treated with nucleoside reverse transcriptase inhibitors (stavudine and lamivudine) and a nonnucleoside reverse transcriptase inhibitor (efavirenz or nevirapine) had significantly higher SBP, pulse pressure, and hemoglobin A_{1c} and more dyslipidemia over 5 years than untreated patients.[158]

Summary

Although the excess burden of chronic kidney disease and end-stage renal disease in African Americans has origins in the disparate burden of cardiovascular risk factors, some unexpected observations are presented as related to faster rates of progression to end-stage renal disease but better survival on dialysis. It is possible that exploration of the healthcare experience of African Americans treated with dialysis could yield insights to provide better management for whites. Investigation of the health implications of sickle cell trait is ongoing, and with the availability of inexpensive genotyping for clinical and research purposes, we can investigate patterns in longitudinal studies in the population. As more research is carried out in diverse population cohorts of adults with HIV, we can gain additional insights into any disparities in the relationship of HIV status with CVDs in African Americans compared with other racial/ethnic groups.

CONTRIBUTION OF GENETICS TO DISPARITIES

As a multifactorial disease, CHD has both environmental and genetic underpinnings, with almost 300 variables identified to interact in unpredictable ways.[159] Conceptually, embracing the idea that genes segregate to populations is the most accurate way to think about genetics in general with respect to multifactorial diseases, including CVD. In studies genotyping populations, correlations have been made between populations and cardiovascular biomarkers, including inflammation, thrombosis, hypertension, lipid profiles, arrhythmia, and cardiac phenotype/left ventricular mass.

Genetic Loci for Inflammation

CRP is a heritable biomarker of systemic inflammation and predictor of CVD at the population level. Recent studies have performed genome-wide association studies (GWASs) of African American populations for genetic relationships to elevated CRP.[160,161] In a GWAS of 8280 African American and 3548 Hispanic American postmenopausal women from the NHLBI SHARe (Single Nucleotide Polymorphism Health Association Resource), a unique triggering receptor expressed on myeloid cells 2 variant was associated with CRP in US minority populations, but genomic loci previously associated with CRP through GWASs of European populations demonstrated consistent patterns of association with CRP in African American and Hispanic American women.[162]

In additional studies from the CARe study (Candidate Gene Association Resource) and race-combined meta-analyses of 29 939 individuals of European descent, 4 loci were identified, 3 of which had been reported previously in populations of European descent.[160] Among African Americans, the fourth locus was the CD36 functional variant rs3211938, which is an extremely rare variant found in those of European descent. These findings were replicated in an independent sample of 8041 African Americans from WHI. In the race-combined meta-analyses, 13 loci reached significance, including 10 previously associated with CRP and 1 previously nominally associated with CRP.[160]

Other studies that have investigated genes associated with elevated CRP levels in diverse populations have found similar gene associations.[160] In an investigation of 3109 African American and 6050 European Americans from the NHLBI ESP (Exome Sequencing Project) and CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) consortia, single-variant tests across candidate loci found an association of *APOE* ε2 rs7214 and higher CRP levels in African Americans.[163] Exome-wide, associations of *HNF1A*, *CRP*, *IL6R*, and *TOMM40-APOE* were confirmed.[163] Although these studies elucidated primarily genes overlapping with other populations, they also elucidated a few novel genes, demonstrating both common and unique potential contributors to elevated CRP levels in African Americans.

Genetic Loci for Thrombosis

Fibrinogen is a major component in the formation of a thrombus, cleaved by thrombin to form fibrin, the most abundant protein present in a blood clot.[164] Higher plasma fibrinogen levels are established markers of coronary artery disease, stroke, peripheral vascular disease, and atrial fibrillation.[165–167] The heritability of plasma fibrinogen concentration as a predictor of CVD has been estimated to be 34% to 50%, with genetic variants so far explaining a small part (<2%) of this variation.[168] Fibrinogen levels have been reported to differ among European Americans, African Americans, and Africans, with the increased levels observed in those of African ancestry.[169–173]

Evidence that genetic variants in the fibrinogen gene itself are related to cardiovascular risk was first identified in a GWAS of 6 population-based studies.[174] Since that time, a meta-analysis of 28 GWASs (which included 8289 African American participants) evaluating clinical outcomes has been published.[168] Twenty-four genome-wide independent signals from 23 loci were significant ($P<5\times10^{-8}$), which included 15 novel associations that accounted for 3.7% of the plasma fibrinogen variation seen.[174] Enrichment analysis of these novel associations identified roles in fibrinogen regulation for the 3 structural genes and pathways related to inflammation, adipocytokines, and thyrotropin-releasing hormone signaling.[168] Although single-nucleotide polymorphisms (SNPs) in a few loci were significantly associated with coronary artery disease, the combined effect of the 24 fibrinogen-associated lead SNPs was not significant for coronary artery disease, stroke, or venous thromboembolism.[168]

The fibrinogen γ chain has 2 splice variants, γA and γ′, resulting in a poly-A signal in intron 9.[175] Because 8% to 15% of total fibrinogen is made of γ′ fibrinogen, the variability of total fibrinogen and fibrinogen γ′ in Africans is only partly explained by known CVD risk factors, with CRP being a major contributor.[173,176] Fibrinogen SNPs account for 1.4% to 3.8% of the variance in total fibrinogen in African Americans[177,178] and 2% of the variance in total fibrinogen in non-Hispanic blacks.[179] Recent studies have investigated the effect of fibrinogen and factor XIII genes on total and γ′ fibrinogen and clot properties in black Africans.[180] Associations among total fibrinogen γ′ levels, rs1049636 (fibrinogen γ chain), and rs2070011 (fibrinogen γA promoter region) were identified.[180] SNPs interacted with total and/or γ′ fibrinogen levels and clot properties in opposite ways, indicating that functionality should be a consideration in determining the effects of SNPs in CVD mechanisms and considerations of risk.[180]

Genetic Loci for Hypertension

The heritability of hypertension documented in adoption, twin, and family studies suggests that 15% to 35% of the correlation may be genetic[181–185]; hypertension onset before the age of 55 occurs nearly 4 times more frequently in individuals with a family history.[186] Together, the heritability of hypertension and increased predominance in African American populations suggest that unique genetic associations may be present in the development of CVD. Although studies of BP associations with cardiovascular phenotypes in European descendants are extensive,[187,188] relatively few studies

have attempted to replicate these observations in African Americans.

In the first GWAS among African Americans, 80 000 SNPs in a discovery sample of 1017 African Americans from the Washington, DC, area were studied.[189] Multiple SNPs in genes encoding a $Na^+/K^+/Ca^{2+}$ exchanger and voltage-dependent calcium channel, respectively, are significant genome-wide for SBP. No gene variants reached significance for association with diastolic BP or with hypertension as a binary trait.[189]

Subsequent genome-wide and candidate gene association studies with SBP and diastolic BP (DBP) using the CARe consortium (consisting of 8591 African Americans) have identified additional genes related to DBP and SBP using 2 different genotyping platforms. None of these variants, however, were replicated in additional African American or European American cohorts, but 3 previously identified European American SNPs did replicate.[190] These findings support the notion that BP among African Americans has genetic influences on SBP and DBP at genetic loci found in European Americans, with potentially unique genes needing validation in other African American populations.[190]

Admixture mapping is a method that can be used to detect disease variants with increased allele frequency differences in ancestral populations. Admixing mapping for SBP and DBP followed by trait marker associated in 6303 unrelated African American participants of the CARe consortium identified 5 significant genomic regions harboring genetic variants contributing to interindividual BP variation.[191] Overall, 3 loci were significantly associated with SBP and 1 with DBP and replicated in multiple large, independent studies of African Americans, including the WHI, Maywood, GENOA (Genetic Epidemiology Network of Arteriopathy), and HUFS (Howard University Family Study), and 1 native African sample (total replication size, 11 882).[191] A novel variant on chromosome 5 (rs7726475) between the *SUB1* and *NPR3* genes was associated with SBP and DBP in the meta-analysis of the replication set.[191] Meta-analyses of the CARe samples with the replication data identified a significant association of rs7726475 and DBP, highlighting the identification of genetic variants missed by GWASs.[191]

In an attempt to replicate the initial GWAS in African Americans described above, an independent sample of 2474 unrelated African Americans in the Milwaukee area (53% women, 47% men) was evaluated.[192] When the top 16 associated SNPs plus the 8 SNPs associated with SBP and DBP in 2 genes (*STK-39* and *CDH-13*) found in European and Amish populations were investigated for their relationship with elevated BP in this African American cohort, no statistically significant differences were identified in African Americans, highlighting the importance of replication studies to validate the findings of GWASs.[192]

Animal and human studies have demonstrated that genetic variations exist, and recent investigations have identified that rare polymorphisms in PCSK9 (proprotein convertase subtilisin/kexin type 9) are associated with BP in African American populations at high risk for CVD.[193] In an analysis of genomic data from the HyperGEN (Hypertension Genetic Epidemiology Network), 2 GWAS SNPs were identified with DBP (rs12048828: β=1.8, P=0.05; rs9730100: β=1.0, P=0.05) but were not significant after correction for multiple testing.[193] Although the DBP did not replicate, an association with SBP (P=0.04) did replicate in REGARDS, suggesting that rare variants in PCSK9 may influence BP among African Americans,[193] laying the groundwork for further validation studies and potential therapeutic considerations given the US Food and Drug Administration progress in approving PCSK9 inhibitors. Finally, in a discovery and meta-analysis that included 21 503 African Americans from across 16 studies, exome-centric single-variant and gene-based tests identified 31 new loci and 3 new genes associated with BP. Notably, these loci are enriched for known variants for other cardiometabolic traits, including dyslipidemia, inflammation, and insulin resistance.[194]

Genetic Loci for Lipid Disorders

The initial GWASs investigating associations of genetic loci with LDL-C, HDL-C, and triglycerides in European ancestry populations identified 19 loci. To expand these associations with circulating lipid levels and CVD, index SNPs were genotyped at 19 loci in NHANES III (n=7159).[195] Analysis of non-Hispanic African Americans, Mexican Americans, and non-Hispanic whites identified the index SNP at 5 loci associated with LDL-C, HDL-C, or triglycerides in all 3 ethnic groups, which allowed the loci to be more finely mapped.[195]

These subsequent studies determined that 22 SNPs in 13 candidate genes were associated with HDL-C, LDL-C, total cholesterol, and triglycerides.[196] Variants in *APOE* (rs7412, rs429358), *PON1* (rs854560), *ITGB3* (rs5918), and *NOS3* (rs2070744) associated with ≥1 of these lipids levels in at least 1 racial/ethnic population were found.[196] Multivariate linear regression analysis of 57 GWAS-identified or well-established lipid-related genetic loci with plasma concentrations of HDL-C, LDL-C, total cholesterol, triglycerides, total cholesterol/HDL-C ratio, and non–HDL-C was performed. With 1 exception (rs3764261 in *CEPT*), single SNP associations and the cumulative effect of multiple SNPs on blood lipid levels varied significantly by race/ethnicity. The findings were consistent for allele frequencies for all of the 57 GWAS-identified or lipid-related genetic loci.[197]

As part of the NHLBI ESP, which included 1652 African Americans from CARDIA, CHS, ARIC, MESA, and WHI, participants who were heterozygous for any of

the 4 mutations in the *APOC3* gene had plasma triglyceride levels that were 39% lower than those who did not. Those same mutations were associated with a lower likelihood of CHD in whites, but the analysis has not yet included African Americans.[198] Another risk allele associated with CVD incidence is *APOL1*. Participants from the JHS who had 2 *APOL1* risk alleles had a doubled (OR, 2.17; $P=9.3\times10^{-4}$) risk for incident CVD compared with those without a risk allele. These findings were replicated in the WHI for a combined OR of 2.12.[199]

Expanding on these initial studies, the Population Architecture Using Genomics and Epidemiology Study was established to determine GWAS-identified variants in diverse population studies. Across racial/ethnic groups, a majority of the 55 of 60 replicated genotype-phenotype associations for HDL-C, LDL-C, and triglycerides in European Americans generalized to African American (48%, 61%, and 57%).[200] For associations that did not generalize, differences in allele frequencies, linkage disequilibrium, and differences in effect sizes may contribute to the differences observed and offer insight into how next associations studies are designed in the future.[200]

To determine the validity of recent GWAS identification of loci/SNPs associated with plasma total cholesterol, LDL-C, HDL-C, and triglycerides, replication studies have been performed in 3 epidemiological samples comprising US non-Hispanic whites, US Hispanics, and African blacks.[201] In African blacks, 7 SNPs were significantly associated with at least 1 lipid trait, and 2 SNPs were associated with >1 lipid trait. These studies demonstrate the mixed results found with these loci with respect to various populations, each with its own allele frequency and contributions to disease.[201]

PCSK9 (encoded by the *PCSK9* gene) is a regulator of LDL receptors, and therapies inhibiting this enzyme have shown promise as a novel, effective therapy for hyperlipidemia. However, in an exome array conducted to genotype >200 000 low-frequency sequences in 14 330 individuals of African ancestry, 4 low-frequency variants in the *PCSK9* gene were identified that had large effects on HDL-C or triglycerides, but none of these were associated with risk for CHD.[202]

Genetic Loci for Vascular Structure and Arrhythmia Risk

GWASs have investigated cardiac structure and systolic function in African Americans recently in the CARe study.[203] Across the 9 cardiac phenotypes, 4 genetic loci reached significance for left ventricular mass, left ventricular internal diastolic diameter, interventricular septal wall thickness, and ejection fraction.[203] None of these were identified in the European ancestry consortium, revealing unique African American variants enriched for 3 signaling pathways involving sonic hedgehog signaling, β-adrenergic signaling, and the oncostatin M signaling pathway.[203] These 3 well-characterized pathways in cardiac remodeling suggest potential mechanisms underlying cardiac mechanisms associated with cardiac disease and potential targets for individualized therapies in individuals with these gene variants.[203]

The *SCN5A* gene, which plays a role in cardiac conduction and repolarization, was studied in relation to QT prolongation in the JHS. A common variant in individuals of African ancestry is the *SCN5A*-1103Y allele, which was found in 15.4% of JHS participants. In the 2% of participants with hypokalemia, there was a statistically significant ($P<0.005$) interaction whereby the allele was associated with prolongation of the QT interval by 15.6 milliseconds ($P=0.02$). In contrast, the association was modest for those without hypokalemia (4.1 milliseconds for each additional copy). The pattern of association between *SCN5A*-1103Y carrier status and hypokalemia was also observed for shorter QRS duration and longer QT, QTc, JT, and JTc intervals, and the findings were more pronounced among those with hypokalemia. The potential for diuretic-induced hypokalemia warrants consideration given the relatively high carrier rate of the *SCN5A*-1103Y allele and its attendant risks for sudden cardiac death.[204]

Summary

Concerns about the potential for the scientific community to misuse genetic information has been a barrier for many African Americans to participate in genetic research.[205,206] However, education efforts that emphasize the value of such information for improving the health of African Americans could overcome many of these barriers. To date, genetic consortia have been the primary source of information on the contribution of genetics to CVD risk. As more cohorts that include racial/ethnic minorities join these collaborative efforts, the prevalence of risk alleles in minority cohorts can be determined, as well as their relationship with incident CVD risks. Finally, if the goals of personalized medicine are realized, these genomic findings may be combined with phenotypic information to provide precise characterizations of individual risk for CVDs.

DISEASE MANAGEMENT AND PREVENTION

Declines in CVD mortality are estimated to be attributable to the combination of the prevention of cardiovascular risk factors and the application of evidence-based therapies.[207] Below, we discuss the challenge of screening for disease in African Americans with subclinical disease imaging, the role of risk calculators for risk strati-

fication, and the evidence for tailored pharmacological management of disease.

Subclinical CVD

Despite a higher burden of traditional risk factors and adverse health behaviors among African Americans, the prevalence of coronary artery calcium (CAC) is typically lower than among whites. Consequently, the inclusion of CAC in risk prediction equations could yield underestimates in African Americans.[208] In the CARDIA study, the prevalence of CAC was 5% in African American women and 11% in African American men compared with 5% in white women and 18% in white men in adults 33 to 45 years old.[209] In MESA participants (mean age, 62 years at baseline), CAC prevalence was highest among white men (70%), followed by African American men (52%), white women (45%), and African American women (37%).[210]

In contrast, African Americans have been reported to have higher common carotid intima-media thickness but comparable internal carotid intima-media thickness compared with whites. According to MESA, the mean common carotid intima-media thickness was 0.91 mm in African Americans compared with 0.87 mm in whites, whereas the mean internal carotid intima-media thickness was similar in African Americans (1.11 mm) and whites (1.13 mm).[211] The strength of association between carotid intima-media thickness and CAC also varies by racial/ethnic group, with the weakest association in African Americans.[211] Genetic predisposition is a possible explanation for weaker associations among African Americans. In MESA, there was a positive association of European ancestry with CAC and common carotid intima-media thickness in African Americans.[212] However, these associations were not replicated among African Americans in the CARDIA and CHS studies.[213,214]

Differences in endothelial dysfunction between African Americans and whites have been observed in some settings but not others. In older adult women, brachial artery flow-mediated dilation was lower in African American compared with white women.[215] Among young men, microvascular function (peak and baseline forearm blood flow) is lower in African American men compared with white women.[216] In addition, nitric oxide bioavailability was lower in African American compared with white patients who were free from CVD risk factors, indicating poorer endothelial function.[217]

Risk Calculators and Stratification

Until the turn of the century, there were no risk prediction tools based on data drawn on or validated in samples containing large numbers of African Americans.[12] A working group convened by the NHLBI on CHD risk prediction[3] demonstrated that the FHS (Framingham Heart Study) risk equation performed reasonably well in predicting CHD outcomes among African American participants in the ARIC study using data from the baseline examination in the 1980s.[218] In response to concerns about the validity of risk equations developed in an era when the CVD risk burden was markedly different, FHS investigators published an updated global risk equation in 2008 that broadened the outcomes beyond CHD.[4] However, the transportability of the equation from the nearly all-white, New England–based cohort to the African American at-risk population remained uncertain.[218] The Reynolds Score improved prediction of ASCVD events by including family history and high-sensitivity CRP measurements in the prediction model. However, similar concerns arose about the generalizability of the score beyond the predominately white and upper-socioeconomic-status populations from which they were developed.[219]

Risk functions for stroke were developed in the 1990s from the FHS[76] and the largely white CHS study.[77] Common predictors of stroke risk across cohorts were BP levels and treatment, prevalent diabetes mellitus, current smoking, atrial fibrillation, left ventricular hypertrophy, and heart diseases. Notably, dyslipidemia is not included in either equation, and there is a substantially heavier weight placed on hypertension as a risk factor. The CHS risk function additionally included measures of physical function and frailty (eg, timed walk). The Framingham Stroke Risk Function demonstrated good discrimination of stroke risk for whites and African Americans in the REGARDS study. However, the risk function likely overestimates stroke risk in the white population because of temporal declines in stroke risk, moving whites out of calibration and moving the higher-risk African Americans into calibration over time.[220] That the risk factors for coronary disease and stroke differ underlies the somewhat modest correlation between the Framingham stroke and Framingham coronary risk functions (Spearman ρ=0.68).[221] These differences may explain the absence of an association between age-adjusted stroke and CHD mortality rates at the state level (Spearman ρ=0.04).[221]

The Pooled Equations published recently by the AHA/American College of Cardiology Working Group directly address several of these possible shortcomings. They are a central pillar for the 4 guidelines simultaneously published to address modern assessment and management of CVD risk[222] and represent the first update on these topics since the publication of the Institute of Medicine's landmark "Guidelines We Can Trust."[222a] The guideline for the assessment of cardiovascular risk features a new risk algorithm developed with data pooled from cohorts that included unprecedentedly large numbers of African Americans. One primary enhancement is that the risk model broadened the set of outcomes of concern beyond CHD to include stroke, a significant

source of disparity in CVD between African Americans and whites.[223–225] The risk algorithm developed from the new guideline data outperformed other risk scores for initial ASCVD events among African Americans (and others) and has gained wide acceptance as a useful, broadly generalizable tool.[224] Its easy accessibility online and its inclusion as a decision-support device through electronic medical record systems enhance its clinical utility. A limitation is that heart failure, another significant source of disparity, is not included. Finally, no risk prediction models are useful for the prediction of silent myocardial infarction, which may occur substantially more frequently among African Americans.

Hence, despite possible shortcomings, the Pooled Equations represent the best effort to date to produce an ASCVD event prediction tool for African American and white adults and has been validated in independent populations such as REGARDS.[226] When this tool is applied to the NHANES data from 2007 to 2010, impressive disparities emerge: In the low-risk category, only 1.4% of African American men have a 10-year CVD risk of <2.5% compared with 18% of white men, 36.5% of African American women, and 47.1% of white women.[226] Frequencies in other risk categories are less disparate; however, more than half (≈54%) of African American men and more than a third (≈34%) of African American women who are without known disease have a 10-year risk of >7.5% for an initial ASCVD event (compared with 44% for white men and 22% for white women), a key cut point for determining the intensity of therapy and the consideration of pharmacological management of CVD risk factors (eg, the use of statins for dyslipidemias).[226]

Recently, a race-specific tool has been developed by JHS investigators[227] using data from the JHS.[228] The investigators developed a tiered approach to select an algorithm that combined optimal prediction performance with ease of application in the primary care setting. They also expanded the relevance of the model to African American populations by including heart failure and stroke among the outcomes. Marginal improvements over the calibrated FHS and the new Pooled Equations were achieved by combining classic risk factors, brain natriuretic peptide, and ankle-brachial index measures. Clinical judgement is most often tested in cases in which the 10-year risk as determined by modern risk equations is neither high (currently meaning >7.5%) nor low (eg, a young person with substantial lifetime risk but with near-term low risk using the Pooled Equations). In such cases, the JHS findings suggest that imaging (echocardiography for left ventricular systolic performance), brain natriuretic peptide, and ankle-brachial index may offer additional useful data.

The authors concluded that, although the JHS-derived equations performed well in predicting disease and marginally improving risk classification over pre-existing equations, they did not offer a substantial improvement in risk prediction among African Americans. This finding underscores (1) the enduring predictive power of the classic risk factors; (2) the fact that we can have reasonable confidence in the Pooled Equations in current wide use for African American and white American populations; (3) that any risk prediction tool is not intended as a substitute for a careful clinical assessment and may not be applicable for every patient; and (4) that a quantum leap forward in CVD prediction for our diverse population awaits further advances in the tools of precision medicine to assess environmental, genetic, and other determinants of risk.

Risk Stratification After ASCVD Events

Few algorithms addressing secondary prevention have come into widespread use because of confounding from treatment. In the REGARDS study, most of the traditional risk factors (eg, hypertension, diabetes mellitus, smoking, atrial fibrillation, left ventricular hypertrophy) play a similar role in predicting incident and recurrent stroke; however, a history of heart disease was associated with an RR of 1.42 (95% CI, 1.20–1.67) for incident stroke but only a nonsignificant (RR, 1.09; 95% CI, 0.85–1.40) risk for recurrent stroke.[229] The substantial (P=0.0002) age-by-race interaction for incident stroke (with HRs of ≈3.0 at age 45 but 1.0 for age 85) was absent (P=0.99) for recurrent stroke, and no difference could be detected between the risk of recurrent strokes in African Americans and whites.[229]

Tailored Pharmacological Therapy in African Americans

Guidelines for pharmacological management of CVD in African Americans do not differ from management in other racial/ethnic groups. However, there are 2 notable exceptions, heart failure and hypertension, in which African American patients may benefit from tailored treatment approaches.

Heart Failure

The American College of Cardiology Foundation and AHA recommend angiotensin-converting enzyme (ACE) inhibitors, β-blockers, and aldosterone antagonists as the standard care in heart failure. Digoxin (Lanoxin) and diuretics are also recommended as adjuncts to control symptoms. Studies conducted in African Americans have documented that this population may have different responses to these medications compared with whites.[230]

ACE inhibitors are recommended for patients with New York Heart Association class I, II, III, or IV heart failure and for patients with left ventricular systolic dysfunction.[231] Despite robust evidence of benefit for ACE inhibitors for reducing mortality, the SOLVD (Studies of Left Ventricular Dysfunction) prevention and treat-

ment trial reported a smaller response to ACE inhibitor therapy (enalapril) in African American compared with white patients who had left ventricular dysfunction. Although SBP and DBP were lower among white patients treated with enalapril and the risk of hospitalization for heart failure was reduced by 44%, there were no significant reductions in any of these metrics among African American patients. Neither racial group received significant survival benefits from Enalapril treatment.[232]

β-blockers are recommended for patients with New York Heart Association class I, II, III, or IV heart failure and for patients with symptomatic and asymptomatic left ventricular systolic dysfunction.[231] Results from BEST (Beta-Blocker Evaluation of Survival Trial) reported a lack of significant survival benefit in African Americans with advanced heart failure when treated with bucindolol (HR, 1.17; 95% CI, 0.89–1.53), whereas there was an evident survival benefit in non–African American patients (HR, 0.82; 95% CI, 0.70–0.96).[233] However, a recent meta-analysis using race-stratified data from COPERNICUS (Carvedilol Prospective Randomized Cumulative Survival), MERIT-HF (Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure), and the US Carvedilol Heart Failure Study found potential survival benefit from bisoprolol, metoprolol, or carvedilol for African American patients with heart failure (RR, 0.67; 95% CI, 0.38–1.16), although this finding is not statistically significant.[234] The absence of significant results may be attributable to the smaller sample size of African Americans in these studies.

Hydralazine plus isosorbide dinitrates is recommended to treat African American patients with left ventricular systolic dysfunction and advanced heart failure (New York Heart Association class III or IV), in addition to β-blockers and ACE inhibitors.[230,231] Data from V-HeFT (Vasodilator-Heart Failure Trial) I showed that, compared with placebo, hydralazine plus isosorbide dinitrates significantly reduced morality in African Americans, whereas such survival benefit was not observed among white patients. In addition, results from the V-HeFT II suggested that white patients received significantly more survival benefit from enalapril compared with hydralazine plus isosorbide dinitrates, whereas this treatment difference was not observed in African American patients. From these results, A-HeFT (African-African Heart Failure Trial) was designed for African American patients with New York Heart Association class III or IV heart failure only. This trial was terminated early because of a significant 43% improvement in survival in the hydralazine plus isosorbide dinitrates treatment group. In addition, the treatment group had a 33% reduction in the rate of first hospitalizations for heart failure and 52% improvement in quality of life.[235] Another potential adjuvant therapy for heart failure in African American patients is supplemental aldosterone antagonist, particularly among those with left ventricular dysfunction. In the Genetic Risk of Heart Failure in African Americans trial, African Americans who had a common (62%) genetic polymorphism in the aldosterone synthase gene (TT genotype in *CYP11B2*) had higher levels of aldosterone and worse survival in heart failure.[236]

It is tempting to conclude that different heart failure therapies should be recommended to African American patients. However, most of the current studies on heart failure therapies included only a limited number of African American patients. Thus, the lack of significant findings is potentially attributable to small sample size. Although further study is needed, standard heart failure therapies should be used in African American patients with heart failure.

Hypertension

Disparities in hypertension control among African Americans are a primary source of disparities in CVDs. Reasons posited for the poorer control of elevated BP among African Americans usually focus on patient-related factors (eg, adherence issues, dietary indiscretion[237]), provider behavior (eg, inertia or poor regimen choices[238,239]), or blunted efficacy of some widely used drug classes (eg, ACE inhibitors) in African Americans.[240] However, the social and cultural environment is equally likely to influence the uptake and sustainability of preventive interventions. By carrying out research to elucidate the complexity of each of these dimensions of hypertension management (ie, social and cultural environment, behavior, pharmacology, pharmacogenetics), we can determine how the overall environmental/biopsychosocial milieu impedes or improves hypertension care and control in African Americans.[241] The ultimate goal is to generate greater precision in our care of African Americans with elevated BP.

There is evidence that race-specific treatment guidelines may be warranted. The British Hypertension Society suggests race-specific guideline recommendations to treat individuals of African descent with diuretics and calcium channel blockers and avoiding treatment with ACE inhibitors and β-blockers because of suppression of the renin-angiotensin system.[242] In the United States, the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure provides specific recommendations for hypertension treatment in African Americans.[243] One such recommendation is that a calcium channel blocker or thiazide-type diuretic be used as initial therapy for African American hypertensive patients.[243] Another that has been met with some controversy is the recommendation that the SBP threshold for diagnosis and treatment should be raised from 140 to 150 mm Hg in adults ≥60 years of age. The Association of Black Cardiologists and the Working Group on Women's Cardiovascular Health cite concerns about these

criteria given the large proportion of African Americans and women affected by hypertension and the risks of end-organ damage resulting from higher levels of BP.[244]

ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) provided the most evidence to support different responses to antihypertensive regimens in African American hypertensive patients.[245] In the ALLHAT trial, patients on chlorthalidone achieved better BP control than patients on other therapies. Namely, SBP was 1 mm Hg lower than in the amlodipine group and 2 mm Hg lower than in the lisinopril group. The lowest risks for outcomes were also observed among those on chlorthalidone. Patients using ACE inhibitors (lisinopril) had a greater risk for stroke (RR, 1.40; 95% CI, 1.17–1.68), combined CVD (RR, 1.19; 95% CI, 1.09–1.30), and heart failure (RR, 1.30; 95% CI, 1.10–1.54) compared with those on chlorthalidone. These treatment differences were far more pronounced in African Americans compared with whites in the trial and make a strong argument in favor of diuretics as an initial drug of choice for treating hypertension in African Americans.[245]

The ALLHAT study also found a higher risk of stroke in African American hypertensive patients treated with ACE inhibitors (lisinopril) compared with a calcium channel blocker (amlodipine; RR, 1.51; 95% CI, 1.22–1.86); this association was not observed in non–African Americans (RR, 1.07; 95% CI, 0.89–1.28).[245] These findings are consistent with results from several other studies. Using pooled results from 30 randomized controlled BP trials from 1968 to 2003, a meta-analysis study showed that there was no evident benefit from ACE inhibitors in achieving DBP goals for African American hypertensive patients. This study also found that African American hypertensive patients did not benefit from 1 particular β-blocker, atenolol, in reducing SBP.[240,246] Similarly, several studies from the Veterans Affairs cooperative provide additional evidence that African American patients respond better to diuretics and calcium channel blockers.[240,247–249]

Although African Americans are shown to be less responsive to ACE inhibitors, ACE inhibitors may offer benefits for African Americans with hypertensive renal disease. In AASK (African American Study of Kidney Disease and Hypertension), which is a comparison study of an ACE inhibitor (ramipril), a calcium channel blocker (amlodipine), and a β-blocker (metoprolol), ACE inhibition showed superior outcomes in relation to renal disease progression. Compared with calcium channel blockers and β-blockers, ACE inhibitors further slowed renal disease progression in African Americans with hypertensive renal disease and proteinuria. ACE inhibitors also offered clinical benefit in the combined end points of glomerular filtration rate events, end-stage renal disease, and death for African American hypertensive patients with renal disease with or without proteinuria.[250]

Adjustments to systems of care characterized by evidence-driven protocols embedded in a team-based, registry-documented, simplified, and tightly orchestrated approach have resulted in control rates of 87.1% in a population that 10 years earlier had a control rate of 43.6%.[251,252] Until truly precise and personalized approaches are developed, a reliance on systems-level approaches may offer huge benefits. These approaches are being rapidly adopted by major caregiving organizations and have gained the endorsement of the AHA and the Centers for Disease Control and Prevention/Department of Health and Human Services–Sponsored Million Hearts Program.[253]

Summary

There is ample evidence that the traditional risk factors for CVD predict clinical outcomes equally well in African Americans and whites. More recent risk prediction equations that include stroke risk are particularly useful for African Americans. The utility of these equations for counseling about disease risks, and ultimately for prevention, can be enhanced when they are coupled with the selection of pharmacotherapies specifically recommended for disease prevention among African Americans.

SOCIAL AND CULTURAL ENVIRONMENT

The social and cultural environment in which African Americans live provides the context that influences the implementation of screening strategies, the application of risk prediction tools in clinical settings, and the uptake of evidence-based therapies.[254–257] Existing research almost universally concludes that the combination of these factors complicates the prevention and management of CVD in African Americans. However, increased awareness and acknowledgement of these barriers have led to investment in strategies that work within the constraints of the environment to promote the cardiovascular health of African Americans.

In 2015, the AHA published a scientific statement addressing the social determinants of risk and outcomes of CVDs.[258] The objective of that statement was to provide a comprehensive review of factors outside of biology that contribute to cardiovascular health and stand in the way of progress toward reaching the 2020 strategic Impact Goals.[258] Unfortunately, African Americans face an overabundance of adverse social and environmental characteristics today in the United States.

African American race in the United States is closely correlated with socioeconomic class. Approximately 26% of African Americans are living in poverty compared with 13% of non-Hispanic whites and 15% of the overall population. The median family income is

Circulation. 2017;136:e393–e423. DOI: 10.1161/CIR.0000000000000534

$43 151 in African American households compared with $66 632 in the US population.[259] On average, education levels are lower and health literacy is compromised. As a result, preventive health resources (healthy foods, safe spaces for physical activity, psychological stability resulting from occupational stability) are not as widely available to the majority of African Americans. Consequently, the challenge of improving health among African Americans requires a broader structural approach.

The AHA's community guide for improving health at the community level[127] discusses evidence-based strategies that can create environments that promote healthy behavior changes and support the health of community members. Given substantial evidence about the contribution of "built environment" factors such as limited access to supermarkets and healthier food choices,[260] an overabundance of advertisements for high-calorie, low-nutrition foods and beverages,[261] and limited access to safe places for physical activity,[262] significant change may require investments in local community infrastructure, large-scale prevention programs, and social policies to support changes. These strategies include the use of policies to influence the built and social environments such as restricting the sale of nonnutritious foods in and around schools, labeling menus, providing incentives for food stores to build outlets in local food deserts, creating safe spaces for physical activity that are monitored to reduce the likelihood of crime, maintaining smoke-free restaurants and public spaces, and setting regulations about noise and air pollution from local businesses. These strategies may be particularly useful for closing the gaps in access and availability for African Americans and other minority communities who face more individual barriers to healthy behavior change and prevention.

There is considerable diversity within the African American community, with a large and growing middle- and upper-class community. However, despite higher education and more socioeconomic resources, health outcomes are still poorer in African Americans whose socioeconomic status is comparable to that of non-Hispanic whites.[263,264] Historical factors, including housing laws and the migration patterns of racial/ethnic groups in the United States, inform the racial composition and structure of neighborhoods and communities. Research indicates that when African Americans live in predominately African American neighborhoods, health outcomes are worse.[265] In the MESA study, the incidence of CVD went up 12% with every 1-SD increase in the degree of neighborhood segregation.[266] Hypothesized reasons include variability in the availability of safe spaces for physical activity or access to healthy foods, which interfere with prevention. On a larger geographic scale, CVD event rates vary widely by geographic location.[224,267] Nationally, 65% of African Americans live in urban regions (counties classified by the National Center for Health Statistics as "large central metro" or "large fringe metro") compared with only 49% of non-Hispanic whites.[268] Stroke mortality rates are 30% higher in rural regions of the country than in urban regions.[269]

Another explanation for persistent disparities across the socioeconomic range in African Americans is the multiple sources of stress and unique sources of stress faced by African Americans. Common sources of stress, job stress and strain, neighborhood-related safety concerns, socioeconomic concerns, and major life events combine with salient sources of stress for African Americans such as perceived discrimination.[270–273] Perceived racial discrimination is known to be associated with all aspects of health, including hypertension,[274] weight gain and obesity,[275] persistent inflammation and other subclinical processes,[276,277] and incident CVD events.[278] The potential for interventions that promote positive psychological health (eg, mindfulness, resiliency) to reduce stress levels may be relevant in improving the health behaviors and ultimately health outcomes of African Americans.[279,280]

The effectiveness of behavior change interventions in the African American community is compromised by a number of factors. As a result of ingrained cultural practices or fears surrounding the healthcare system because of historical abuses, African Americans may be less likely to follow physician recommendations for behavior change.[281] One of the most striking examples of the confluence of cultural practices, socioeconomic conditions, and attitudes among African Americans compromising the effectiveness of therapy is in management of the obesity epidemic. Although it is possible that lower levels of overall education or health literacy may contribute to the lack of understanding of the relationship among dietary intake, body weight, and chronic disease risk[282] or that food purchasing habits are influenced by socioeconomic circumstances,[259] it is equally likely that traditional preferences may be more influential than socioeconomic status in predicting food purchasing behaviors.[283] According to some reports, African American families and social networks do not promote positive lifestyle changes.[213,284,285] The attitudes and behaviors that some African Americans have about weight may also influence the adoption of dietary guidelines.[75,286–288]

As a result, although individual weight-loss interventions show variable effectiveness, all weight-loss interventions are systematically less effective in African Americans according to a meta-analysis.[289] In a review of weight-loss interventions, studies that were successful included cultural adaptation and, even more important, constituent involvement; that is, adaptation informed by the experience of the target group.[290] Conducting interventions in locations that are valued in the African

American community can enhance their uptake; 1 review reports that 70% of interventions conducted in African American faith-based organizations achieved success in weight reduction.[291]

Summary

Although African Americans face a number of social and structural barriers to positive cardiovascular health, a number of strengths of the cultural environment can be leveraged to disseminate behavioral health interventions (eg, the central role of the church for reaching women and older adults). Some of these barriers can be addressed by targeting the macroenvironment via policy changes at the federal (eg, Affordable Care Act), state (eg, cigarette smoking bans), and local (eg, food availability in schools) levels. Doing so could create environments to support and sustain positive health behavior changes. However, finding strategies that reach younger African Americans and men with disease prevention messages is a challenge that must be met to change the trajectory of health in the African American community.

THE NEXT STEPS

To make progress toward our goal of promoting health equity and achieving the AHA 2020 Impact Goals, the significant burden of morbidity and mortality from CVD among African Americans must be reduced. Doing so will require collaborations across multiple disciplines, both within and outside of the traditional umbrella of healthcare providers given the complex historical, social, and economic reasons why African Americans experience poorer cardiovascular health. Efforts to carry out high-quality research studies should be supplemented by additional research on the dissemination and implementation of effective interventions to modify health behaviors and to mitigate CVD risks. New initiatives such as the precision medicine initiative (ie, All of Us) provide a unique opportunity to learn more about individual genotypes and how therapies can be tailored to be maximally effective for African Americans.

However, such research will be effective only if the diverse spectrum of the African American population is represented. Despite the wealth of information that we have about the CVD burden in African Americans from surveillance studies and longitudinal cohort studies, African American men and socioeconomically disenfranchised (including homeless) populations remain less likely to participate in research. Although these population subgroups are difficult to reach in any racial/ethnic group, historical abuses by the healthcare system (eg, Tuskegee Syphilis Study), which spurred a lasting culture of mistrust, may further alienate African Americans. At present, life expectancy among African American men is shorter than all for other racial/ethnic groups, and health outcomes among the socioeconomically disenfranchised in the United States mirror those of populations in the developing world. Identifying strategies to reach these groups with preventive and clinical care needs to be a high priority.

One strategy to begin to repair trust and to increase the engagement of all African Americans in the healthcare system is to diversify the workforce of healthcare professionals. In a recent report from an NHLBI Think Tank on Strategies to Promote Health Equity, a priority was placed on ensuring a diverse workforce of clinicians and researchers by creating unique transdisciplinary training programs.[271] From the research perspective, identifying and addressing the numerous barriers to cardiovascular health requires input from disciplines as broad as anthropology, public policy, and education, as well as traditional disciplines such as medicine, epidemiology, and psychology. On the clinical side, healthcare providers who demonstrate cultural competency in their interactions and a willingness to try to understand the perspectives of the patients they treat will yield higher-quality interactions. Although such skills are relevant for all healthcare providers, the infusion of the patient-facing medical fields with more African American clinicians (eg, physicians, physician assistants, and nursing professionals) may speed the uptake of these important principles. However, efforts to increase the number of clinical providers must begin with programming that builds the pipeline of African American students who are interested in selecting medicine as a career and who are prepared to succeed.

With the considerable amount of information that we have about the prevalence and sources of disparities in cardiovascular health between African Americans and other racial/ethnic groups, we stand poised to address and eliminate those disparities with contributions from professionals with expertise in basic science and pharmacology, clinical medicine, and public health. By successfully translating findings from across disciplines, scientists and practitioners from other disciplines can apply innovative strategies to improve the cardiovascular health of African Americans.

FOOTNOTES

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. specifically, all members of the writing group are required to complete and submit a disclosure questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on June 23, 2017, and the American Heart Association Executive Committee on August 21, 2017. A copy of the document is available at http://professional.heart.org/statements by using

Circulation. 2017;136:e393–e423. DOI: 10.1161/CIR.0000000000000534

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The American Heart Association requests that this document be cited as follows: Carnethon MR, Pu J, Howard G, Albert MA, Anderson CAM, Bertoni AG, Mujahid MS, Palaniappan L, Taylor HA Jr, Willis M, Yancy CW; on behalf of the American Heart Association Council on Epidemiology and Prevention; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; and Stroke Council. Cardiovascular health in African Americans: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e393–e423. doi: 10.1161/CIR.0000000000000534.

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DISCLOSURES

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Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
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This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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